Impact of a ring fitted cap on insertion time and adenoma detection: a randomized controlled trial

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Abstract

Background and Aims:

Devices for flattening colon folds can improve polyp detection at colonoscopy. However, there are few data on the endoscopic ring fitted cap (EndoRings, EndoAid, Caesarea, Israel). We sought to compare adenoma detection with EndoRings with that of standard high-definition colonoscopy.

Methods:

A single-center randomized controlled trial of 562 patients (284 randomized to EndoRings and 278 to standard colonoscopy) at 2 outpatient endoscopy units in the Indiana University Hospital system. Adenoma detection was the primary outcome measured as adenoma detection rate (ADR) and adenomas per colonoscopy (APC). We also compared sessile serrated polyp detection rate (SSPDR), insertion times, withdrawal times, and ease of passage through the sigmoid colon.

Results:

EndoRings was superior to standard colonoscopy in terms of APC (1.46 vs 1.06, p=0.025) but there were no statistically significant differences in ADR or SSPDR. Mean withdrawal time (in patients with no polyps) was shorter and insertion time (all patients) was longer in the EndoRings arm by 1.8 minutes and 0.75 minutes, respectively. One provider had significantly higher detection with EndoRings and contributed substantially to the overall results.

Conclusions:

EndoRings can increase adenoma detection without significant increase in procedure time, but the effect varies between operators. EndoRings slows colonoscope insertion.

Introduction

Endoscopic ring fitted caps (EndoRings, EndoAid, Caesarea, Israel) and Endocuff (Olympus Corporation, Center Valley, Pa) are essentially competing mucosal exposure devices for improving polyp detection during colonoscope withdrawal. Endocuff has been tested in multiple randomized controlled trials[1-6] and meta-analyses suggests it improves the adenoma detection rate (ADR) by an average of 7% [7]. There are fewer data available regarding EndoRings. In a tandem study, use of EndoRings was associated with a reduced miss rate for colorectal adenomas [8]. In an observational study, EndoRings was associated with a trend toward improved detection and shorter withdrawal time [9]. In a 4-arm randomized controlled trial comparing standard high definition colonoscopy to Endocuff with high-definition colonoscopy to EndoRings with high definition colonoscopy to the full-spectrum endoscopy colonoscope (FUSE), Endocuff was a dominant strategy in that it led to shortened colonoscope insertion time compared with EndoRings, and improved detection [6]. In a large European trial, EndoRings did not improve detection [10].

We performed a separate industry-sponsored single center randomized controlled trial comparing EndoRings on high definition colonoscopes with standard high definition colonoscopy alone. Unlike our previous 4-arm randomized controlled trial, we did not force withdrawal times to be equal in this study, but rather allowed them to vary as allowed by the examination technique of

individual examiners. Because the benefits of endoscopic adjuncts are often operator-dependent, we include the results for individual endoscopists.

Methods

We performed a randomized controlled clinical trial comparing high-definition Olympus colonoscopes to high-definition Olympus colonoscopes with EndoRings in patients undergoing colonoscopy for screening or surveillance indications.

Patients were recruited by study coordinators as they presented for colonoscopy at 1 of 2 outpatient endoscopy units in our system and were randomized in a 1:1 ratio after signing an informed consent. The randomization list was computer generated and stored with a central coordinator. After recruitment, the list was accessed by a coordinator not involved in recruitment to assign randomization. Patients presenting for screening or surveillance colonoscopy and able to provide a written informed consent were deemed eligible for the study. Patients were excluded if they were age <50 years, were referred for polypectomy or a previously incomplete colonoscopy, who had a personal history of colorectal cancer or inflammatory bowel disease, familial adenomatous polyposis, serrated polyposis syndrome, or a prior colon resection. A total of 9 board certified gastroenterologists participated in the study. The study was approved by the Institutional Review Board at Indiana University on January 19, 2018. Patients were recruited between January 2018 and September 2018. The trial was registered on ClinicalTrials.gov (NCT03418662).

Patients were prepared for colonoscopy using a variety of split dose bowel preparations. Patients were sedated in the overwhelming majority of cases with propofol (monitored anesthesia care) administered by an anesthesiologist. Insertion time consisted of the time from insertion of the colonoscope into the anus until the appendiceal orifice was visualized and was measured with a stopwatch. The stopwatch was stopped during insertion if a polyp was identified and removed during insertion, but was not stopped for any washing or suctioning that occurred during insertion. Water instillation during insertion was used at the discretion of the endoscopist. Withdrawal time was measured with a stopwatch, and consisted of the time from when the cecum was cleaned and inspection began until retroflexion was completed in the rectum. We did not subtract time for washing or suctioning during withdrawal, or biopsy or polypectomy as we have in previous studies [6, 11]. For each polyp detected, we recorded the size, shape, location, method of removal, and final pathologic diagnosis. At the end of the procedure, patients were asked to rate the procedure on a scale of 0 to 10 with 10 being the worst imaginable pain and 0, no pain. We also asked the endoscopists to rate the ease of passing sigmoid on a 1 to 5 scale, with 5 being very difficult and 1 very easy.

Statistical Analysis

The primary endpoint was adenoma detection, measured as adenoma detection rate (ADR, number of individuals with ≥1 conventional adenoma) and the number of conventional adenomas per colonoscopy (APC). Secondary endpoints included sessile serrated polyp (SSP) detection rate (SSPDR, number of individuals with ≥1 SSP), SSPs per colonoscopy, insertion time, withdrawal time in patients with normal colonoscopies, and ease of passage through the sigmoid

colon. Ease of sigmoid passage was rated on a subjective 5-point scale by the endoscopist where 1 = no resistance and 5 = marked resistance to passage.

We assumed that ADR might increase from 25% in the standard arm to 35% in the EndoRings arm. A 2-group Chi-Square test with a 0.05 one-sided significance level would have 80% power to detect an absolute difference of 10% ADR between the 2 groups when the sample size in each group is 259 or 518 overall. Assuming an approximate 10% drop out rate, we planned to enroll 569 subjects.

The EndoRings and standard groups were compared for differences using chi-square tests for gender, race, cecum reached, fellow participation, and presence of at least one polyp, adenoma, or sessile serrated polyp. Wilcoxon Rank Sum tests were used to compare the groups for differences in age, Boston Bowel Preparation Score (BBPS), ease of passage through the sigmoid colon, patient comfort score during colonoscopy, and insertion and withdrawal times. Negative binomial models for count data were used to compare groups for differences in the number of polyps, adenomas, and SSPs. A 5% significance level was used for each test. All analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC).

In a secondary analysis, the EndoRings and standard groups were compared for differences in the frequency of at least one polyp, adenoma, or SSP using logistic regression and for differences in polyp, adenoma, and SSP counts using negative binomial models. The logistic regression and negative binomial models included indication in the models as a covariate. A 5% significance level was used for each test.

The study was sponsored by EndoAid. All study data were collected and analyzed at our site. The study sponsor designed the trial in conjunction with D.K.R. and was given access to the completed data set but had no input to and did not view this manuscript before publication.

Results

There were 569 subjects randomized, including 287 to EndoRings and 282 to standard colonoscopy. There were 7 subjects randomized but excluded from all analyses, including 1 case that was aborted due to inadequate bowel preparation (standard arm), 3 patients diagnosed with inflammatory bowel disease during the procedure (all three EndoRings), 1 patient excluded because of age < 50 years (standard arm), 1 patient who was assigned a previously randomized number (standard arm), and 1 patient who was randomized before the provider was approved for the study (standard arm). The intent-to-treat analysis included 562 subjects (284 EndoRings and 278 in the standard arm).

Table 1 is a comparison of patient and procedure characteristics between the groups, which showed no significant differences. There was a trend ($p = 0.059$) toward fewer screening and more surveillance patients in the EndoRings arm.

Mean insertion time was longer with EndoRings (Table 1), including cases when no fellow was involved in the colonoscope insertion process. The difference in mean insertion time between the 2 arms was 0.75 minutes, or 14% longer with EndoRings compared with standard colonoscopy. Ease of passage through the sigmoid colon on a scale of 1 through 5 (5 = most difficult) was

worse for EndoRings, mean 2.51 (1.43) vs 1.60 (1.04), $p < 0.001$. Self-reported patient comfort scores were similar in both groups (Table 1), but nearly all patients were sedated with propofol.

In patients with no polyps detected, mean withdrawal time was shorter using EndoRings by 1.8 minutes (Table 1). Total withdrawal time was not reduced with EndoRings, possibly because more polyps were removed.

Table 2 shows the detection endpoints for the study in the intent-to-treat analysis. For the primary endpoint of adenomas per colonoscopy (APC), EndoRings were superior to standard colonoscopy, 1.46 (2.69) vs 1.06 (1.83), $p = 0.025$. There was no difference in the adenoma detection rate, and no difference in the serrated targets, or individual targets when separated by location in the colon (data not shown). Because of the trend toward more surveillance and fewer screening patients in the EndoRings arm, we performed regression analysis controlling for indication. In the intent-to-treat analysis, APC remained higher with EndoRings ($p = 0.048$), but polyps per colonoscopy (PPC) did not ($p = 0.06$; data not shown). Table 2 shows that the size distribution of adenomas detected by EndoRings and standard colonoscopy were similar ($p = 0.92$), suggesting gains in detection with EndoRings across polyp sizes.

Table 3 shows the results for the individual nine doctors for the primary endpoint of APC. One of the nine physicians had a significantly higher APC, and one had a trend toward increased APC, but three of the 9 endoscopists performed colonoscopy on relatively small numbers of patients. When the results from physician 6 were removed from the analysis, there was no difference in detection for the remaining eight physicians combined for any endpoint.

Of patients randomized to EndoRings, the device was removed to pass the instrument to the cecum in 8.8% of cases (Table 2). This ranged from 0% to 17% of procedures among individual endoscopists.

Discussion

In this study we found that EndoRings were associated with an improvement in adenomas per colonoscopy (APC), while simultaneously associated with a reduction in withdrawal time. We had previously demonstrated in an uncontrolled study in our center that EndoRings was associated with a trend toward improved detection yet with significantly shorter withdrawal time. In a randomized controlled trial comparing Endocuff to standard colonoscopy, we found that Endocuff produced a reduction in withdrawal time almost identical to that observed in this study (1.93 minutes) and a trend toward improved detection [11]. That study was much smaller and was not powered to demonstrate improved detection. Thus, the primary result of the study was positive in that EndoRings produced both improved detection, and at the same time, shorter withdrawal time.

Two caveats about the result seem significant. The first is that the insertion time with EndoRings was prolonged compared with standard colonoscopy. This was not observed in previous studies with Endocuff, which actually shortened insertion time [5]. The explanation is certainly the bulkier shape of EndoRings, which at times had to be pushed through the sigmoid colon. The worse scores with EndoRings for difficulty passing the sigmoid in this study are consistent with that impression. Additionally, the endoscopist removed the device in almost 9%

of cases, similar to a recent report [10], but a higher fraction than seen in previous studies [6, 8], including from our own site [6, 9]. This may reflect increased difficulty when EndoRings is used by general endoscopists. A second important finding is that the detection improvements were not seen even numerically for all examiners. Thus, the benefits observed in the study were operator dependent. All of the examiners had significant experience with EndoRings before the onset of the study, and the use of the device is similar to Endocuff and intuitive in its nature. At this time, we are not certain of the reason why the detection benefits demonstrated significant operator dependence. However, the results suggest that individual examiners might need to make measurements with EndoRings to determine if the increase in insertion time associated with the device is worth any improvement they are able to measure in detection.

Strengths of our study include the randomized design, large size, reporting the results by individual examiners, and that the examiners were general endoscopists. Limitations include single center design and inability to blind the endoscopists regarding whether EndoRings was being used. However, the latter limitation is common to essentially all detection studies. In addition, although the comfort scores were not different between arms, they would not reasonably be expected to differ in participants sedated with propofol. It would be of interest to test whether add on devices such as EndoRings or Endocuff affect patient comfort when colonoscopy is performed unsedated or with light sedation.

In summary, our results suggest that across a number of colonoscopists in an academic practice, all of whom were clinical gastroenterologists, EndoRings produced an improvement in APC without an increase in overall procedure times. These results reinforce our recent findings

observed with Endocuff, that devices on the end of the colonoscope have the potential to improve lesion detection without increasing withdrawal time [11, 12]. In this regard, their effects are unique. Based on extensive experience with EndoRings and Endocuff, our impression (which is supported by evidence [6]) is that Endocuff is easier to use during colonoscopy, and the only available controlled comparison suggested that it performed better than EndoRings from the perspectives of both insertion and detection. Overall, the results of this study and others support the use of fold-flattening devices on the end of the colonoscope during routine colonoscopy and indicate that Endocuff is a dominant device. Depending on its cost, EndoRings may also warrant evaluation by individual examiners, perhaps particularly for younger patients with a lower risk of significant sigmoid diverticular disease.

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Table 1. Comparison of patient demographics, preparation scores, procedure times, comfort scores and ease of sigmoid passage

	EndoRings (n=284)	**Standard (n=278)**	***P* value**
Age, mean (SD)	61.9 (8.1)	61.0 (7.9)	.224
Female, n (%)	131 (46)	142 (51)	.240
White, n (%)	233 (83)	222 (81)	.475
Screening indication, n (%)	143 (50)	162 (58)	.059
Cecal intubation	281 (99)	277 (100)	.523
Procedures where device was removed, n (%)	25 (8.8)	-	-
Fellow participation, n (%)	39 (14)	26 (10)	.108
Boston Bowel Preparation Scale (BBPS) score, n (%)			
3-5	6 (2)	5 (<2)	
6-7	35 (12)	39 (14)	
8-9	239 (85)	235 (84)	
Total BBPS score, mean (SD)	8.50 (1.05)	8.47 (1.11)	.905
Mean insertion time, minutes (SD)	6.3 (4.4)	5.5 (3.4)	.004
Mean inspection time – patients with no polyps only, minutes (SD)	7.9(2.2)	9.7(2.9)	<.001
Mean total withdrawal time (all patients), minutes (SD)	11.8 (6.1)	12.8 (5.9)	.01
Mean total procedure time (all patients), minutes (SD)	19.4 (8.2)	19.5 (7.9)	.898
Patient comfort score, mean (SD)	0.47 (1.1)	0.36 (0.9)	.415
Ease of passage through sigmoid, mean (SD)	2.5 (1.4)	1.6 (1.4)	<.001

n, number of patients; SD, standard deviation,

Table 2. Detection endpoints

	EndoRings (n=284)	**Standard (n=278)**	***P* value**
Polyps per colonoscopy, PPC, Mean (SD)	2.29 (3.09)	1.82 (2.19)	.025
Polyp detection rate, PDR (%)	199 (70)	188 (68)	.532
Adenomas per colonoscopy, APC, Mean (SD)	1.46 (2.69)	1.06 (1.83)	.025
Adenoma detection rate, ADR (%)	143 (50)	124 (45)	.172
Sessile serrated polyps per colonoscopy, SSPPC, Mean (SD)	0.24 (0.84)	0.18 (0.70)	.366
Sessile serrated polyp detection rate, SSPDR (%)	35 (12)	25 (9)	.201
Adenomas detected by size, number (%)			**.970**
1-5 mm	**314 (76)**	**222 (76)**	
6-9 mm	**74 (18)**	**50 (17)**	
≥10 mm	**28 (7)**	**19 (7)**	

n, number of patients; SD, standard deviation

Table 3. Individual provider adenomas per colonoscopy data

Doctor	N	EndoRings	N	Standard	*P* value
1	17	1.76 (1.71)*	35	1.60 (2.10)	.785
2	9	0.78 (1.09)	12	0.83 (1.03)	.906
3	30	0.73 (1.28)	29	0.59 (0.95)	.607
4	53	1.55 (2.99)	48	0.81 (1.51)	.068
5	4	2.25 (2.63)	1	4.00	.562
6	52	2.98 (3.97)	47	1.19 (1.84)	.002
7	52	0.79 (1.23)	47	1.19 (2.36)	.264
8	51	1.18 (2.70)	48	1.04 (1.91)	.730
9	16	0.50 (1.10)	11	0.64 (1.21)	.766

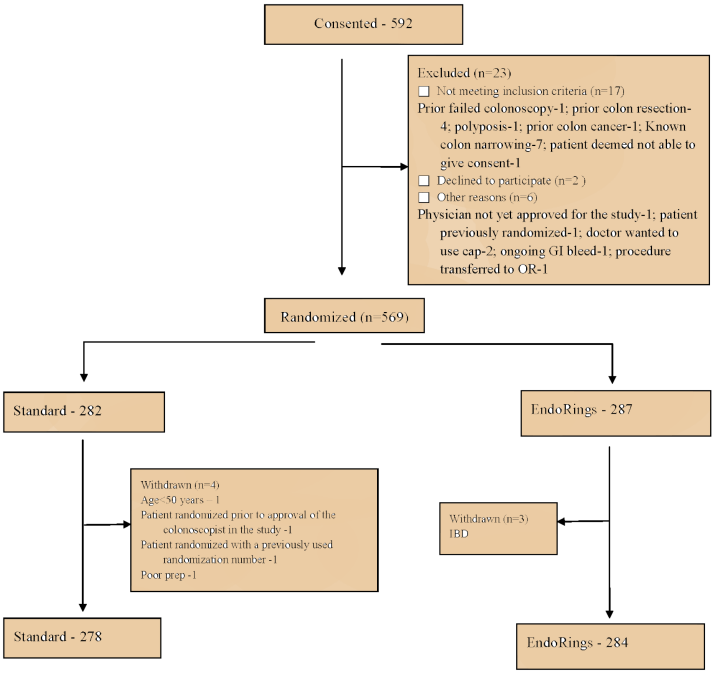
N = number of patients

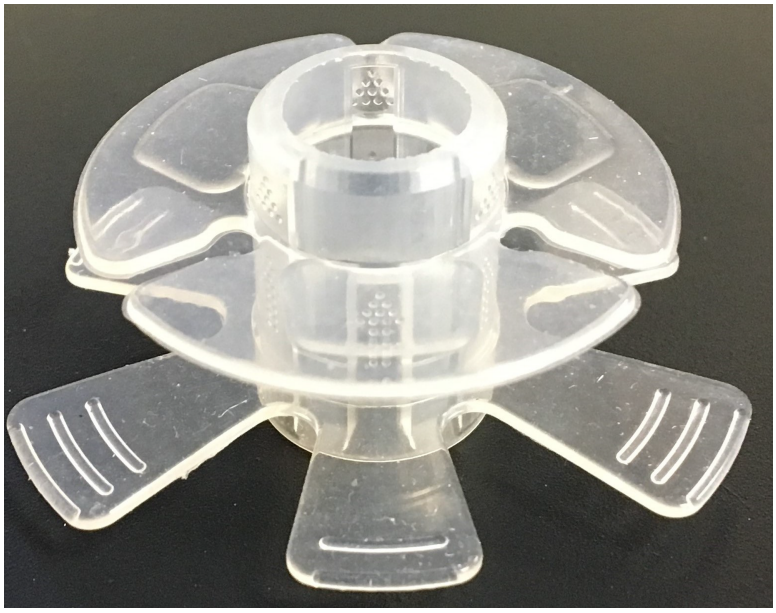
* = mean adenomas per colonoscopy (standard deviation)

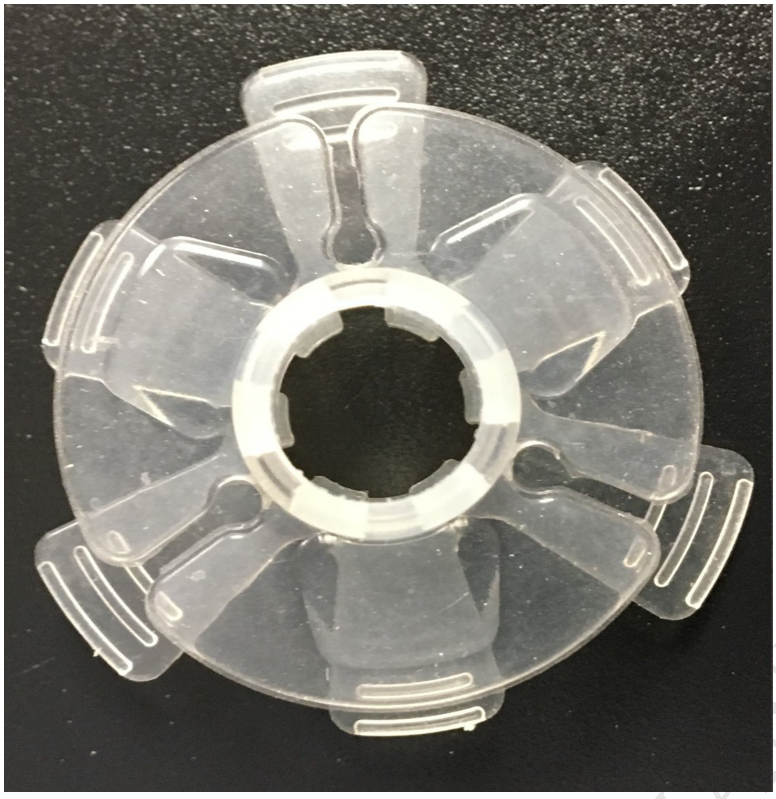
Figure legends

Figure 1. Flow of patients through the study.

Figure 2. EndoRings viewed from the side (A) and from the top (B).







Acronyms

ADR adenoma detection rate

APC adenomas per colonoscopy

BBPS Boston Bowel Preparation Score

DKR Douglas K. Rex

FUSE full spectrum endoscopy colonoscope

PDR polyp detection rate

SD standard deviation

SSP sessile serrated polyp

SSPDR sessile serrated polyp detection rate

SSPPC sessile serrated polyps per colonoscopy